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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,803	11/14/2005	Giuseppe Arpaia	279737US0PCT	1463

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EXAMINER	
XU, XIAOYUN	

ART UNIT	PAPER NUMBER
4112	

NOTIFICATION DATE	DELIVERY MODE
07/09/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/556,803	ARPAIA ET AL.	
	Examiner	Art Unit	
	ROBERT XU	4112	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/14/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summary

1. This is the initial Office action based on the 10/556,803 application filed on November 14, 2005.

2. Claims 1-14 are pending and have been fully considered.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.,* 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over MIKSIL [Journal of Chromatography B, Vol. 739, pages 109-116 (2000)] in view of CALDWELL [US Patent No. 5,516,703].

In regard to Claim 1, MIKSIK teaches application of Poloxamer in capillary electrophoretic separation of a protein (abstract). MIKSIK teaches that capillary

electrophoresis methods suffer from protein analytes sticking to the capillary wall and low selectivity, particularly if closely related proteins/fragments are subjected to electromigration separations (page 109, left col., lines 6-10). Therefore, MIKSIK applies Poloxamer in capillary electrophoretic separation to increase the resolution (page 115, left col., Lines 12-17). MIKSIK also performs reverse phase HPLC and compares the results with capillary electrophoresis (*2.3. HPLC*). MIKSIK does not apply Poloxamer in reverse phase HPLC, therefore, the separation profile of the HPLC is different from the capillary electrophoresis (Figure 1, A, B). CALDWELL teaches that Poloxamer (Pluronic surfactants) are triblock copolymers with the structure PEO-PPO-PEO (where "PEO" is poly(ethylene oxide) and "PPO" is poly(propylene oxide) (Col. 2, lines 13-17). CALDWELL further teaches that Poloxamer having a hydrophobic center block with hydrophilic end blocks can be used to coat hydrophobic surfaces. The center blocks are adsorbed onto the surface, with the end blocks extending from the surface and waving freely in a seaweed-like fashion. The coverage of the hydrophobic center blocks and the action of the end blocks effectively blocks the nonspecific adsorption sites and creates a nonadsorbing surface to certain substances such as proteins (Col. 2 lines 4-12). At the time of the invention, it would have been obvious to one of ordinary skill in the art to apply Poloxamer in reverse phase HPLC with reasonable expectation that this would reduce the protein loss caused by the surface adsorption of the pathway. This method for reducing the protein loss is within the ordinary ability of one of ordinary skill in the art based on teachings of CALDWELL.

In regard to Claim 2, simple dilution of protein sample to a level acceptable for the chromatographic system is well-known in the art.

In regard to Claims 3-4, the chromatographic analysis taught by MIKSIK detects the quantity and purity of the protein (Figure 1B).

6. Claims 5 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over MIKSIL [Journal of Chromatography B, Vol. 739, pages 109-116 (2000)] in view of CALDWELL [US Patent No. 5,516,703] as applied to Claims 1-4 above, and further in view of LEE [US Patent No. 5,656,730]

In regard to Claim 5, as has been discussed in Claim 1, MIKSIL teaches reverse phase HPLC. LEE teaches using size-exclusion chromatography to purify the monomeric single chain antigen binding protein with Pluronic F-68 in the solution (Col. 10, lines 29-30 and 37-39).

In regard to Claim 10, LEE teaches using size-exclusion chromatography to purify the monomeric single chain antigen binding protein with Pluronic F-68 in the solution (Col. 10, lines 29-30 and 37-39).

7. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over CALDWELL [US Patent No. 5,516,703] in view of MIKSIL [Journal of Chromatography B, Vol. 739, pages 109-116 (2000)] as applied to Claims 1-4 above, and further in view of WEN [Analytical Biochemistry, Vol. 240, pages 155-166 (1996)].

In regard to Claim 6, WEN teaches that Stem cell factor (SCF) is a dimeric glycoprotein. WEN studies the SCF by size-exclusion chromatography (page 159, left col., lines 12-18, Figure 4). As discussed in Claim 1 above, CALDWELL and MIKSIL teach that Poloxamer reduces the protein loss caused by sticking to the wall of the pathway. At the time of the invention, it would have been obvious to one of the ordinary skill in the art to add Poloxamer to the dimeric glycoprotein sample for size exclusion chromatography with seasonable expectation that this would reduce the loss of the protein caused by adsorption to the wall of the pathway.

8. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over MIKSIL [Journal of Chromatography B, Vol. 739, pages 109-116 (2000)] in view of CALDWELL [US Patent No. 5,516,703] as applied to Claims 1-4 above, and further in view of WU [Journal of Endocrinology, Vol. 137, pages 59-68 (1993)].

In regard to Claim 7, WU teaches that FSH from bovine pituitary glands is isolated by size exclusion (gel filtration) chromatography (abstract). As discussed in Claim 1 above, CALDWELL and MIKSIL teach that Poloxamer reduces the protein loss caused by sticking to the wall of the pathway. At the time of the invention, it would have been obvious to one of the ordinary skill in the art to add Poloxamer to the FSH sample for size exclusion chromatography with seasonable expectation that this would reduce the loss of the protein caused by adsorption to the wall of the pathway.

9. Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over MIKSIL [Journal of Chromatography B, Vol. 739, pages 109-116 (2000)] in view of CALDWELL [US Patent No. 5,516,703] as applied to Claims 1-4 above, and further in view of ARDUINI [Protein Science, Vol. 8, pages 1867-1877 (1999)].

In regard to Claims 8 and 9, ARDUINI teaches that Interferon bata-1a is isolated by size exclusion (gel filtration) chromatography (abstract). As discussed in Claim 1 above, CALDWELL and MIKSIL teach that Poloxamer reduces the protein loss caused by sticking to the wall of the pathway. At the time of the invention, it would have been obvious to one of the ordinary skill in the art to add Poloxamer to the Interferon bata-1a sample for size exclusion chromatography with seasonable expectation that this would reduce the loss of the protein caused by adsorption to the wall of the pathway.

10. Claims 11and 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over MIKSIL [Journal of Chromatography B, Vol. 739, pages 109-116 (2000)] in view of CALDWELL [US Patent No. 5,516,703] as applied to Claims 1-4 above, and further in view of TOSCHI [European Journal of Biochemistry, Vol. 252, pages 108-112 (1998)] and EK-RYLANDER [Biochemistry Journal, Vol. 321, pages 305-311 (1997)].

In regard to Claim 11, the concentration of 100 µg/ml is equivalent to 0.01%. TOSCHI teaches that elution buffer of 0.01% Pluronic F68 and 50 mM sodium acetate, pH 4 is used in protein purification by chromatography (page 109, left col., lines 28-33).

In regard to Claim 12, TOSCHI teaches that elution buffer of 0.01% Pluronic F68 and 50 mM sodium acetate, pH 4 is used in protein purification by chromatography

(page 109, left col., lines 28-33). TOSCHI does not teach that elution buffer comprises 0.1% Pluronic F68. However, 0.1% of Pluronic F68 has been commonly used in the art. For example, EK-RYLANDER teaches using 0.1% Pluronic F68 in protein solution. Differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT XU whose telephone number is (571)270-5560. The examiner can normally be reached on Mon-Thur 7:30am-5:00pm, Fri 7:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Barbara Gilliam can be reached on (571)272-1330. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

RX

/Brian Sines/

Primary Examiner, Art Unit 1797